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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
MAHATAN, CHANNING	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 01/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/891,517	KURANE ET AL.	
	Examiner	Art Unit	
	Channing S Mahatan	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 April 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *55-81* is/are pending in the application.

4a) Of the above claim(s) *60-67* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *55-59 and 68-81* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1 Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

APPLICANTS' ARGUMENTS

Applicants' arguments, filed 29 April 2004, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Newly submitted claims 60-67 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

Claims 60 and 61 correspond to original claim 44, which was previously restricted to Group XII; drawn to an eighth method, PCR-based. Original claim 44 had the separate and distinct limitation of:

"determining an initial concentration of the amplified target gene from a percentage of a change in an intensity of fluorescence occurred as a result of hybridization between said primer or amplified nucleic acid amplified using said primer and said amplified target nucleic acid"

Claim 62 correspond to original claim 46 which were restricted to Group XIV; drawn to a tenth method, PCR-based (qtPCR). Original claim 46 had the separate and distinct limitation of:

"measuring an intensity of fluorescence in a reaction system in which said probe and said target gene or amplified nucleic acid have not hybridized with each other and also an intensity of fluorescence in said reaction system in which said probe and said target nucleic acid or amplified nucleic acid are hybridized with each other; and then calculating percentage of a decrease of said former intensity of fluorescence from said latter intensity of fluorescence"

Claims 63-67 correspond to original claims 51 and 52, which were restricted to Group XV; drawn to data analysis methods. Original claims 51 and 52 had the separate and distinct limitation of:

"correcting an intensity value of fluorescence in a reaction system..."

and formulas (1)-(7).

Since Applicants have received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 60-67 are withdrawn from consideration as being directed to a non-elected invention. See 37 C.F.R. § 1.142(b) and M.P.E.P. § 821.03.

CLAIMS UNDER EXAMINATION

Claims herein under examination are claims 55-59 and 68-81.

SEQUENCE COMPLIANCE

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a) (1) and (a) (2). See, for example, Figures 3 & 5; page 46, lines 17-19; page 104, lines 3, 8, 10, 16; page 105, line 3; page 109, line 4; page 117, line 17; page 120, line 20; page 123, lines 10-19; page 124, lines 3-8; etc. of the specification. However, this application fails to comply with the requirements of 37 C.F.R. § 1.821 through 1.825 because Figures 3 & 5; page 46, lines 17-19; page 104, lines 3, 8, 10, 16; page 105, line 3; page 109, line 4; page 117, line 17; page 120, line 20; page 123, lines 10-19; page 124, lines 3-8; etc do not have SEQ ID NOs. cited along with each sequence in the specification or Figures. Applicants are also reminded that SEQ ID NOs. are not required in Figures per se, however, the corresponding SEQ ID NOs. then are required in the Brief Description of the Drawings section in the specification. Applicants are also reminded that a CD-ROM sequence listing submission may replace the paper and computer readable form sequence listing copies. Applicants are required to submit a new computer readable form,

sequence listing, a paper copy for the specification, statements under 37 C.F.R. § 1.821(f) and (g). Applicants are given the same response time regarding this failure to comply as that set forth to respond to this office action. A complete response to this office action includes compliance with this sequence rule compliance requirement. Failure to respond to this requirement may result in abandonment of the instant application or a notice of a failure to fully respond to this office action.

Claims Rejected Under 35 U.S.C. § 112 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

NEW MATTER

Claims 55-59 and 68-81 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 55 and all claims dependent therefrom are rejected under 35 U.S.C. § 112, first paragraph. The limitation "wherein said determining and amplifying are conducted at the same time" is considered new matter. The specification is devoid of the teaching that said steps are or can be conducted at the same time. It is noted the specification does provides for the detection of a plurality of nucleic acids at the same time (pages 37-38, lines 20-25 and 1-5, respectively), and the determination of the concentration of many target nucleic acids at the same time (page 61,

lines 20-23), and the amplification of a gene by PCR or the like and detection of the gene at the same time (page 62, lines 19-21). However, there does appear to be support for the above limitation such that "determining the initial concentration of a target gene" and "amplifying a target gene" are conducted at the "same time". Therefore, the above amendments are considered NEW MATTER.

Claims Rejected Under 35 U.S.C. § 112 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 55-59 and 68-81 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

VAGUE AND INDEFINITE

Claim 55 and all claims dependent therefrom recite the first step of "determining the initial concentration of a target gene" and a subsequent step (final step) of "determining the initial amount of the target gene..." which is confusing. For instance, if the "initial concentration" of the target gene is known (i.e. amount/volume) then it would appear that the "initial amount" of the target gene would already be known. Therefore, it is unclear what apparent information would be gathered by "determining the initial amount of the target gene" when the concentration is known. Clarification of the metes and bounds, via clearer claim language is requested.

Claim 59 recites the limitation "said probe is labeled at a modification portion other than a 5' end phosphate group or a 3' end OH group thereof with said fluorescent dye" which is

considered vague and indefinite. The language "modification portion" implies a set of parameters/criteria for the identification and thus for the probe to be labeled at. Applicants' can resolve this issue by pointing out the parameters/criteria that the "modification portion" of the probe encompasses. Clarification of the metes and bounds, via clearer claim language, is requested.

Claim 71 recites the language "wherein the distance between said bases... is 1 to 20" which is considered vague and indefinite. It is unclear if the recited numerical values are an indication of the actual number of bases or some other determined value representing a measured physical distance. Applicants can resolve this issue by indicating the units represented by "1 to 20". Clarification of the metes and bounds, via clearer claim language, is requested.

LACK OF ANTECEDENT BASIS

Claim 57 recites the limitation "wherein said probe is labeled at an end portion thereof with said fluorescent dye" which lacks proper antecedent basis. Claim 55, which claim 57 depends from, does not identify or make any indication of a "said fluorescent dye". Therefore, the above limitation recited in claim 57 lacks proper antecedent basis.

OBJECTION TO SPECIFICATION

The amendment filed 29 April 2004 is objected to under 35 U.S.C. § 132 because it introduces new matter into the disclosure. 35 U.S.C. § 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

Amendment to page 66, lines 4-11 (filed 29 April 2004):

> "In the present invention, the nucleic acid probe is hybridized to the target nucleic acid as described above. The intensity of fluorescence emitted from the fluorescent dye is measured both before and after the hybridization, and an increase or decrease in fluorescence intensity after the

> hybridization is then calculated. As the increase or decrease is proportional to the concentration of the target nucleic acid, the concentration of the target nucleic acid can be determined."

Applicants contend support for the above amendment to replace "increase" with "increase and decrease" can be found on pages 6-7 of said 'Substitute Specification', which asserted as discussing "decrease and an increase in emission". However, this citation in the 'Substitute Specification' fails to indicate any discussion of an "increase in emission", rather only "decrease in emission" is discussed. For clarification of the record regarding the amendments filed corresponding to page 66, lines 4-11:

The 'Original specification' (filed 27 June 2001) and the 'Substitute Specification' recited:

> "The present invention, the nucleic acid probe is hybridized to the target nucleic acid as described above. The intensity of fluorescence emitted from the fluorescent dye is measured both before and after the hybridization, and a decrease in fluorescence intensity after the hybridization, and a decrease in fluorescence intensity after the hybridization is then calculated. As the decrease is proportional to the concentration of the target nucleic acid, the concentration of the target nucleic acid can be determined."

The 'Preliminary Amendment' (filed 19 November 2001) attempted to incorporate the following changes into the specification:

> "In the present invention, the nucleic acid probe is hybridized to the target nucleic acid as described above. The intensity of fluorescence emitted from the fluorescent dye is measured both before and after the hybridization, and a change in fluorescence intensity after the hybridization is then calculated. As the change is proportional to the concentration of the target nucleic acid, the concentration of the target nucleic acid can be determined."

The 'Office Action' (mailed 29 January 2004; page 3, lines 7-15) indicated the replacement of the term "decrease" with the language "change" is interpreted to encompass both "decrease and increase", however, no such disclosure or contemplation for these amendments can be found. Therefore, in the absence of proper support Applicants are required to cancel the new matter in the reply to this Office Action.

Additionally, Applicants are to note the term "gene" has been replaced with "gent" in the amendment to page 7, lines 5-9 in the 'Response' filed 29 April 2004 (page 2, line 5). This appears to be a typographical error and thus Applicants are requested to correct this error in the subsequent amendment.

ACTION IS FINAL AS NECESSITATED BY AMENDMENT

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See M.P.E.P. § 706.07(a). Applicants are reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. § 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

EXAMINER INFORMATION

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 C.F.R. § 1.6(d)). The CM1 Fax Center number is either 571-273-8300.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Channing S. Mahatan whose telephone number is (571) 272-0717. The Examiner can normally be reached on M-F (8:30-5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D., can be reached on (571) 272-0718.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify Applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables Applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Examiner Initials: GSM

Date: January 22, 2005

Ardin H. Marschel 1/24/05
ARDIN H. MARSCHEL
PRIMARY EXAMINER